

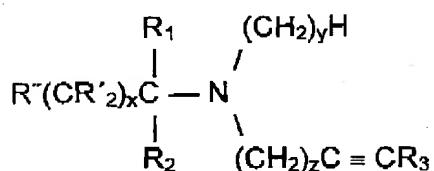
Appl. No. 09/600,125
 Amdt. dated May 10, 2004
 Reply to Office action of February 11, 2004

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-51 (Previously cancelled).

52. (Previously added) A method for enhancing the activity of an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I



wherein

x is an integer ranging from 0 to 13;

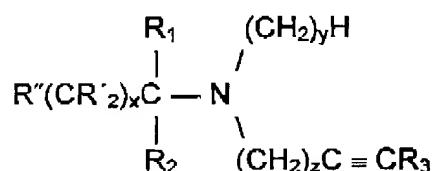
y is an integer ranging from 0 to 5;

z is 1;

R₁, R₂ and R₃ are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R'' are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof.

53. (Previously amended) A method for increasing the sensitivity of a tumor to an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I



Appl. No. 09/600,125
 Amdt. dated May 10, 2004
 Reply to Office action of February 11, 2004

wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

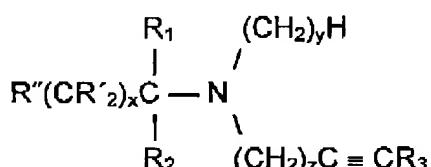
z is 1;

R₁, R₂ and R₃ are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof.

54. (Previously added) A method according to claim 53 wherein the tumor is a drug resistant tumor.

55. (Currently amended) A method for protecting normal cells from the cytotoxic effects of an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I



wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1;

R₁, R₂ and R₃ are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof

with the proviso that when the propargylamine is not R-deprenyl or R-desmethyldeprenyl, the normal cells are not peripheral neurons.

56. (Previously added) A method according to claim 52 wherein y is 1.

57. (Previously added) A method according to claim 56 wherein the propargylamine is R-2 heptyl-methyl propargylamine (R-2HMP).

Appl. No. 09/600,125

Amndt. dated May 10, 2004

Reply to Office action of February 11, 2004

58. (Previously added) A method according to claim 52 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N methylpropargylamine; N-(1-Decyl) N-methylpropargylamine; N-(1-Undecyl) N methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N methylpropargylamine; (R)-N-(2-Heptyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Decyl) N methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

59. (Previously added) A method according to claim 52, wherein y is 0.

60. (Previously added) A method according to claim 59 wherein the propargylamine is R 2-heptyl-propargylamine (R-2 HPA).

61. (Previously added) A method according to claim 59 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) propargylamine; N-(2-Propyl) propargylamine; N-(1-Butyl) propargylamine; N-(1-Pentyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Heptyl) propargylamine; N-(1-Octyl) propargylamine; N-(1-Nonyl) propargylamine; N-(1-Decyl) propargylamine; N-(1-Undecyl) propargylamine; N-(1-Dodecyl) propargylamine; (R)-N-(2-Butyl) propargylamine; (R)-N-(2-Pentyl) propargylamine; (R)-N-(2-Hexyl) propargylamine; (R)-N-(2-Heptyl) propargylamine; (R)-N-(2-Octyl) propargylamine; (R)-N-(2-Decyl) propargylamine; (R)-N-(2-Undecyl) propargylamine; and (R)-N-(2-Dodecyl) propargylamine.

62. (Previously added) A method according to claim 52 wherein the propargylamine is R-deprenyl.

63. (Previously added) A method according to claim 52 wherein the propargylamine is R desmethyldeprenyl.

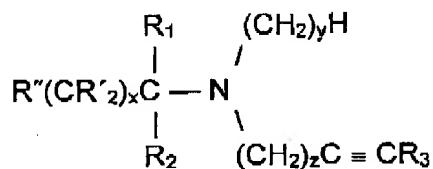
64. (Previously added) A method according to claim 52 wherein the animal is a human.

Appl. No. 09/600,125
 Amdt. dated May 10, 2004
 Reply to Office action of February 11, 2004

65. (Previously added) A method for enhancing the activity of an antineoplastic drug comprising administering an effective amount of Rasagiline to an animal in need thereof.

66. (Previously added) A method according to claim 52 wherein the propargylamine is a chiral compound and is the R-enantiomer.

67. (Previously amended) A method for treating cancer comprising administering an antineoplastic drug and an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I



wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1;

R₁, R₂ and R₃ are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

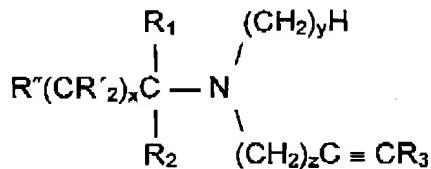
R' and R'' are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof, with the proviso that the propargylamine is not R-deprenyl, R-desmethyldeprenyl or Rasagiline.

68. (Previously added) A method according to claim 67 wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophosphamide, adriamycin, daunomycin, and 5-fluorouracil.

69. (Previously amended) A method according to claim 67 wherein the propargylamine is a chiral compound and is the R-enantiomer.

70. (Previously amended) A pharmaceutical composition for treating cancer comprising an antineoplastic drug and an effective amount of a propargylamine of the general formula I:

Appl. No. 09/600,125
 Amdt. dated May 10, 2004
 Reply to Office action of February 11, 2004



wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1;

R₁, R₂ and R₃ are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R'' are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof,
 with the proviso that the propargylamine is not R-deprenyl, R-desmethyldeprenyl or Rasagiline.

71. (Previously added) A pharmaceutical composition according to claim 70 wherein y is 1.

72. (Previously added) A pharmaceutical composition according to claim 71 wherein the propargylamine is R-2-heptyl-methyl propargylamine (R-2HMP).

73. (Previously added) A pharmaceutical composition according to claim 71 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) N methylpropargylamine; N-(2-Propyl) N-methylpropargylamine; N-(1-Butyl) N methylpropargylamine; N-(1-Pentyl) N-methylpropargylamine; N-(1-Hexyl) N methylpropargylamine; N-(1-Heptyl) N-methylpropargylamine; N-(1-Octyl) N methylpropargylamine; N-(1-Nonyl) N-methylpropargylamine; N-(1-Decyl) N methylpropargylamine; N-(1-Undecyl) N-methylpropargylamine; N-(1-Dodecyl) N methylpropargylamine; (R)-N-(2-Butyl) N-methylpropargylamine; (R)-N-(2-Pentyl) N methylpropargylamine; (R)-N-(2-Hexyl) N-methylpropargylamine; (R)-N-(2-Heptyl) N methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Decyl) N-methylpropargylamine; (R)-N-(2-Undecyl) N methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

74. (Previously added) A pharmaceutical composition according to claim 70, wherein y is 0.

Appl. No. 09/600,125
Arndt, dated May 10, 2004
Reply to Office action of February 11, 2004

75. (Previously added) A pharmaceutical composition according to claim 74 wherein the propargylamine is R-2-heptyl-propargylamine (R-2HPA).

76. (Previously added) A pharmaceutical composition according to claim 74 wherein said propargylamine is selected from the group consisting of N-(1-Propyl) propargylamine; N-(2-Propyl) propargylamine; N-(1-Butyl) propargylamine; N-(1-Pentyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Heptyl) propargylamine; N-(1-Octyl) propargylamine; N-(1-Nonyl) propargylamine; N-(1-Decyl) propargylamine; N-(1-Undecyl) propargylamine; N-(1-Dodecyl) propargylamine; (R)-N-(2-Butyl) propargylamine; (R)-N-(2-Pentyl) propargylamine; (R)-N-(2-Hexyl) propargylamine; (R)-N-(2-Heptyl) propargylamine; (R)-N-(2-Octyl) propargylamine; (R)-N-(2-Octyl) propargylamine; (R)-N-(2-Decyl) propargylamine; (R)-N-(2-Undecyl) propargylamine; and (R)-N-(2-Dodecyl) propargylamine.

77. (Previously added) A pharmaceutical composition according to claim 70 wherein the propargylamine is a chiral compound and is the R-enantiomer.

78. (Cancelled) A pharmaceutical composition according to claim 70 wherein the propargylamine is R-deprenyl.

79. (Cancelled) A pharmaceutical composition according to claim 70 wherein the propargylamine is R-desmethyldeprenyl.

80. (Previously added) A pharmaceutical composition for treating cancer comprising an antineoplastic drug and Rasagiline.

81. (Previously Added) A method according to claim 53, wherein y is 1.

82. (Previously Added) A method according to claim 55, wherein y is 1.

83. (Previously Added) A method according to claim 53, wherein the propargyamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N-methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N-methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N-methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N-methylpropargylamine; N-(1-Decyl) N-methylpropargylamine; N-(1-Undecyl) N-methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N-methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N-methylpropargylamine; (R)-N-(2-Heptyl) N-methylpropargylamine; (R)-N-(2-Octyl) N

Appl. No. 09/600,125

Amtd. dated May 10, 2004

Reply to Office action of February 11, 2004

methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Decyl) N-methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

84. (Previously Added) A method according to claim 53, wherein the propargylamine is selected from R-2-heptyl-methyl propargyamine (R-2HMP) and R-2-heptyl-propargylamine (R-2-HPA).

85. (Previously Added) A method according to claim 55, wherein the propargyamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N-methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N-methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N-methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N-methylpropargylamine; N-(1-Decyl) N-methylpropargylamine; N-(1-Undecyl) N-methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N-methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N-methylpropargylamine; (R)-N-(2-Heptyl) N-methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Decyl) N-methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

86. (Previously Added) A method according to claim 55, wherein the propargylamine is selected from R-2-heptyl-methyl propargyamine (R-2HMP) and R-2-heptyl-propargylamine (R-2-HPA).

87. (Previously Added) A method according to claim 53, wherein the propargylamine is a chiral compound and is the R-enantiomer.

88. (Previously Added) A method according to claim 55, wherein the propargylamine is a chiral compound and is the R-enantiomer.

89. (Previously Added) A method according to claim 53, wherein the animal is human.

90. (Previously Added) A method according to claim 55, wherein the animal is human.

91. (Previously Added) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatin and its derivatives and the topoisomerase interactive agents.

Appl. No. 09/600,125
Amdt. dated May 10, 2004
Reply to Office action of February 11, 2004

92. (Previously Added) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatinum and its derivatives and the topoisomerase interactive agents.

93. (Previously Added) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatinum and its derivatives and the topoisomerase interactive agents.

94. (Previously Added) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosourea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl -1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophosphamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.

95. (Previously Added) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosourea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl -1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophosphamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.

96. (Previously Added) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosourea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl -1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophosphamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.

97. (Previously Added) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophosphamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.

Appl. No. 09/600,125
Amtd. dated May 10, 2004
Reply to Office action of February 11, 2004

98. (Previously Added) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophosphamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.

99. (Previously Added) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophosphamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.

100. (Previously Added) A method according to claim 57, wherein the antineoplastic drug is cis-platinum.

101. (Previously Added) A method according to claim 60, wherein the antineoplastic drug is cis-platinum.

102. (Previously Added) A method according to claim 84, wherein the antineoplastic drug is cis-platinum.

103. (Previously Added) A method according to claim 86, wherein the antineoplastic drug is cis-platinum.

104. (Previously Added) A method according to claim 67, wherein the cancer involves cells mutant in p53.

105. (Previously Added) A method according to claim 104, wherein the cancer is selected from the group consisting of leukemias, lymphomas (Hodgkins and non-Hodgkins), lung and colorectal carcinomas, melanomas, ovarian cancer, testicular cancer and breast cancer.

106. (Previously Added) A method according to claim 55, with the further proviso that the propargylamine is not rasagiline.